REMARKS

Claims 1, 2, 4, 5-10, 13, 14, 16-25, 27-37 and 41, 42 remain in the application. Claims 3, 11, 12, and 40 have been cancelled.

The drawings have been objected to under 37 C.F.R. § 1.84. Upon indication that the present application is in condition for allowance, Applicant will provide corrected drawings to place the drawings in compliance with 37 C.F.R. § 1.84.

Claims 32-37 stand rejected under 35 U.S.C. § 112, first paragraph, as it is stated that the specification while being enabling for the treatment of recurrence of migraine, allegedly does not reasonably provide enablement for preventing migraine recurrence. Applicant respectfully submits that it was well known prior to the priority date of the present invention that eletriptan is useful in the prevention of migraine recurrence. In particular, the specification (page 1, lines 16-17) references WO 00/06161 which includes data demonstrating that eletriptan is useful not only in the treatment of migraine but also in the treatment of migraine recurrence. Accordingly, Applicant respectfully submits that claim 32-37 are sufficiently enabled and that the rejection under 35 U.S.C. § 112, first paragraph, be removed.

Amended Claim 19, which depends from amended claim 1, was rejected as it is alleged that the coating composition in claim 19 contains language that was excluded by the language of amended claim 1. Applicant respectfully submits that the pharmaceutical composition set forth in amended claims includes a permeable layer "comprising an acrylic copolymer". Applicant respectfully submits that the pharmaceutical composition can contain the optional elements set forth in the claim. Accordingly, Applicant submits that claim 19 is in proper form and depends correctly from amended claim 1.

Claim 40 was rejected under 35 U.S.C. § 102(a) as being anticipated by Jackson, et al. (WO00/06161). Applicants have cancelled claim 40 thereby rendering moot any objection thereto.

Claims 1, 4, 15, 27, 32, and 40-42 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Cherukuri, et al. (US 2002/0044962).

Applicant respectfully submits that Cherukuri, et al. does not anticipate any of the claims of the present application. In particular, Cherukuri, et al. disclose, as the examiner notes, a composition comprising a drug incorporated into an erodible polymer. The polymer is dispersed throughout the composition. In contrast, present claim 1 defines a pharmaceutical composition comprising a pharmaceutically acceptable seed having a layer of eletriptan hydrobromide dispersed thereon and a water-permeable acrylic copolymer. Accordingly, since Cherukuri, et al. do not teach or disclose each and every element of the claimed invention as arranged in the claim, the claims are clearly patentable over Cherukuri, et al., and reconsideration of the claims is respectfully requested.

In the Office Action, it is stated that "Applicants' experimental data provided in the **132 declaration** prepares the drug eletriptan by layering the drug cores onto sugar spheres and this aspect differs form [sic] the prior art of Jackson. Thus, Applicants' composition in the declaration differs form [sic] the Jackson composition. Also contrary to Applicants' statement ethyl cellulose is required in Stevens, is it respectfully noted that there is a disclosure of a formulation having EUDRAGIT has the sole polymer."

Applicants respectfully submit that the experiment was carried by layering eletriptan onto sugar spheres as it was not possible to apply the teaching of Jackson directly to eletriptan since cores of eletriptan could not be made by extrusion-spheronization. This is why a coated sugar core was used (see paragraph 5 of the Declaration).

WO 00/106161 (page 7, line 29) proposes that eletriptan, or a salt thereof, can be administered in the form of a sigmoidal releasing pellet by applying the technology disclosed in US 5,112,621 in relation to diltiazem. US Patent 5,112,621 discloses a coating mixture comprising ethyl cellulose and an acrylic resin. The applicant submits that it should be noted that the reference in WO 00/06161 to "sigmoidal releasing pellets (e.g. as referred to in US Patent no. 5,112,621)" clearly refers to the new invention disclosed in US 5,112,621 ("The

present invention provides a sustained-release pharmaceutical composition which comprises microparticles comprising an active principle, said microparticles being coated with a coating mixture comprising ethyl cellulose and an acrylic resin...") and not to a particle coated solely with Eudragit RS which is mentioned in US 5,112,621 solely for comparative purposes.

As was previously presented applicant has conducted experiments to assess whether the teaching of WO 00/106161 is correct in respect of its proposal that a sigmoidal release composition of eletriptan could be prepared by substituting eletriptan for diltiazem in the composition disclosed by US 5,112,621. The results of these experiments were summarized in Declaration form. The results demonstrate that when the coating disclosed in US 5,112,621 is applied to drug cores containing eletriptan hemisulphate, rather than diltiazem, a sigmoidal pattern of drug release is not obtained.

Claims 1-10, 15-39, 41 and 42 stand rejected under35 U.S.C. § 103(a) as allegedly being unpatentable over Jackson, et al. in view of Cherukuri, et al.

As stated above, WO 00/106161 (page 7, line 29) proposes that eletriptan, or a salt thereof, can be administered in the form of a sigmoidal releasing pellet by applying the technology disclosed in US 5,112,621 in relation to diltiazem. US Patent 5,112,621 discloses a coating mixture comprising ethyl cellulose and an acrylic resin. The applicant submits that it should be noted that the reference in WO 00/06161 to "sigmoidal releasing pellets (e.g. as referred to in US Patent no. 5,112,621)" clearly refers to the new invention disclosed in US 5,112,621 ("The present invention provides a sustained-release pharmaceutical composition which comprises microparticles comprising an active principle, said microparticles being coated with a coating mixture comprising ethyl cellulose and an acrylic resin...") and not to a particle coated solely with Eudragit RS™ which is mentioned in US 5,112,621 solely for comparative purposes.

Also as stated above, Cherukuri, et al. disclose a composition comprising an erodible polymer disposed throughout the composition. This is in contrast to the presently claimed

invention which would define the "water-insoluble" polymer which surrounds the drug substance.

Instant claim 1 relates to a pharmaceutical composition comprising eletriptan, or a salt thereof, which is capable of achieving a sigmoidal pattern of controlled drug release by use of a water insoluble, permeable coating consisting of one or more acrylic copolymer(s) containing trimethylammoniumethylmethacrylate groups and, optionally, one or more of a plasticiser, an anti-tacking agent or a wetting agent.

None of the cited documents disclose such a pharmaceutical composition. In particular, a pharmaceutical composition comprising a seed having a first layer of eletriptan hydrobromide dispersed on the seed and a second water-permeable acrylic copolymer layer.

None of the cited documents disclose a formulation of eletriptan, or a salt thereof, which is capable of delivering a sigmoidal pattern of controlled drug release. The objective problem solved by the present application in light of any of the cited art is thus the provision of a formulation of eletriptan, or a salt thereof, capable of delivering such a pattern of sigmoidal drug release. The problem is solved by the invention as presently claimed, as demonstrated by Example 6 in the application.

None of the cited prior art suggests that a controlled release coating consisting of acrylic copolymers alone (or in conjunction with one or more standard pharmaceutical excipients selected from a plasticiser, an anti-tacking agent and a wetting agent) would solve the objective problem outlined above. In particular, ethyl cellulose is an essential feature of the disclosure of US 5,112,621 and there is no suggestion that it may be dispensed with. US 5,112,621, therefore, teaches away from instant claim 1. The applicant submits claim 1, as currently amended, is patentable under 35 U.S.C. § 103(a) over the cited references, either separately or in the combination cited by the Examiner, and respectfully requests withdrawal of the rejection. The applicant further submits that currently pending claims 2-10 and 15-42 all of which incorporate the novel and unobvious features of claim 1, are all patentable under 35 U.S.C. §

103(a) over the cited references, either separately or in the combination cited by the Examiner, and respectfully request withdrawal of the rejection.

In view of the above arguments the applicant's further request withdrawal of the objection to claims 11-14 which the Examiner previously deemed allowable if not dependent on a rejected base claim.

In view of the amendments set forth herein and remarks above, the applicant respectfully submits that the pending claims are fully allowable, and solicits the issuance of a notice to such effect. If a telephone interview is deemed to be helpful to expedite the prosecution of the subject application, the Examiner is invited to contact applicant's undersigned attorney at the telephone number provided.

Respectfully submitted,

Dated: 10/21/05

David R. Kurlandsky
Registration No. 41,505
Warner-Lambert Company
2800 Plymouth Road
Ann Arbor, MI 48105
Telephone: (734) 622-7304
Facsimile: (734) 622-1553